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EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,170	KAWAOKA, YOSHIHIRO	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-11 and 32-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-6,8-11 and 32-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

Applicant's Amendment

1) Acknowledgment is made of Applicant's amendment filed 06/10/05 in response to the non-final Office Action mailed 02/08/05.

Status of Claims

2) Claims 1, 3, 5 and 12 have been amended via the amendment filed 06/10/05.

Claims 2 and 7 have been canceled via the amendment filed 06/10/05.

New claim 36 has been added via the amendment filed 06/10/05.

Claims 1, 3-6, 8-14 and 16-36 are pending.

Claims 1, 3-6, 8-11 and 32-36 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The rejection of claims 2 and 7 made in paragraph 13(c) of the Office Action mailed 02/08/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is moot in light of Applicant's amendment to the claims.

6) The rejection of claim 2 made in paragraph 14 of the Office Action mailed 02/08/05 under 35 U.S.C. § 102(b) as being anticipated by Martin *et al.* (*Virology* 241: 101-111, 1998, already of record) or Brandli *et al.* (*J. Biol. Chem.* 263: 16283-16290, 1988, already of record) as evidenced by Doyle *et al.* (US 20040132164) and Ito *et al.* (*J. Virol.* 71: 3357-3362, 1997), is moot in light of Applicant's amendment to the claim.

Rejection(s) Withdrawn

7) The rejection of claims 1, 8-11 and 32-35 made in paragraph 11 of the Office Action mailed

01/15/04 and maintained in paragraph 12 of the Office Action mailed 07/13/04 and paragraph 10 of the Office Action mailed 02/08/05 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is withdrawn in light of Applicant's amendment to the base claim.

8) The rejection of claim 1 and those dependent therefrom made in paragraph 14 of the Office Action mailed 07/13/04 and maintained in paragraph 11 of the Office Action mailed 02/08/05 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn in light of Applicant's amendment to the base claim.

9) The rejection of claim 1 made in paragraph 13(a) of the Office Action mailed 02/08/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the claim.

10) The rejection of claims 34 and 35 made in paragraph 13(b) of the Office Action mailed 02/08/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the base claim.

11) The rejection of claims 3-6, 8-11 and 32-35 made in paragraph 13(c) of the Office Action mailed 02/08/05 under 35 U.S.C § 112, second paragraph, as being indefinite, is withdrawn in light of Applicant's amendment to the base claim.

12) The rejection of claims 1, 8, 32, 34 and 35 made in paragraph 15 of the Office Action mailed 02/08/05 under 35 U.S.C. § 102(b) as being anticipated by Matta *et al.* (*Parasitol Res.* 85: 293-299, 1999), is withdrawn in light of Applicant's amendment to the base claim.

Rejection(s) Maintained

13) The rejection of claims 1, 3, 4, 8, 32, 34 and 35 made in paragraph 14 of the Office Action mailed 02/08/05 under 35 U.S.C. § 102(b) as being anticipated by Martin *et al.* (*Virology* 241: 101-111, 1998, already of record) or Brandli *et al.* (*J. Biol. Chem.* 263: 16283-16290, 1988, already of record) as evidenced by Doyle *et al.* (US 20040132164) and Ito *et al.* (*J. Virol.* 71: 3357-3362, 1997), is maintained for reasons set forth therein and herebelow.

New claim 36 has been added now to this rejection.

Applicant acknowledges that the infectivity of one of Martin's transfectant viruses on a mutant ricin-resistant MDCK cell was greatly reduced compared to wild-type MDCK cells and that these resistant MDCK cells have a 70 to 75% reduction in cell surface sialic acid.

With regard to Brandli's teachings, Applicant submits that Brandli *et al.* disclose that a ricin-resistant MDCK cell line (MDCKII-RCAD and wild-type cells bind wheat germ agglutinin (specific for N-acetylglucosamine and N-acetylneuraminic acid), conconavalin A (specific for mannose) and *H. pomatia* agglutinin (N-acetylgalactosamine), which binding was unaffected by exogalactosylation (page 16286). Applicant contends that wild-type cells did not contain significant amounts of N-acetylglucosamine (assessed by *B. simplicifolia* agglutinin binding) while mutant cells bound *B. simplicifolia* agglutinin, which could be eliminated by exogalactosylation. In contrast to wild-type cells, Applicant states that mutant cells did not bind peanut lectin (specific for terminal galactose linked to N-acetylgalactosamine) and that mutant cells had decreased binding to (70 to 75%) *Limax flavus* agglutinin (LFA, a lectin which binds sialyl residues in a non-glycosidic linkage specific manner). Brandli *et al.* are said to conclude that MDCKII-RCAr cells are deficient in the addition of galactose residues to N- and O-linked glycans.

With regard to Ito *et al.*, Applicant submits that Ito *et al.* incubated frozen sections of avian allantoic cells, avian amniotic cells, and MDCK cells with digoxigenin labeled *Maakia amurensis* (MAA) lectin or *Sambucus nigra* (SNA) lectin to characterize the lectin binding specificity of those cells. Applicant states that those cells were not grown in the presence of lectin, e.g., to select for cells that were resistant to lectin growth inhibition.

With regard to Doyle *et al.*, Applicant states that Doyle *et al.* describe compositions and methods for enzymatic reduction of adhesion by microorganisms to cells, tissues, extracellular matrix teeth and/or dental prosthesis. Applicant submits that Doyle *et al.* mention that polyphenol oxidase and the asparaginase are effective in reducing influenza A virus attachment to sialic acid containing red blood cells.

Applicant concludes that none of the cited references discloses a mutant mammalian or avian cell with reduced levels of N-acetylneuraminic acid or N-glycolylneuraminic acid.

Applicant's arguments have been carefully considered, but are not persuasive. Ito *et al.* and Doyle *et al.* are as-evidenced-by type references cited to document that the properties of the mutant cell are inherent from the teachings Martin *et al.* or Brandli *et al.*

Martin *et al.* taught isolated mutant MDCK RCA^r (Madin-Darby canine kidney) cells that have 70-75% reduced levels of cell surface sialic acid receptors specific for influenza virus. The

mutant cells were susceptible to infection by influenza virus (see abstract; page 106; and Figures 4 and 5).

Brandli *et al.* taught isolated mutant MDCK (Madin-Darby canine kidney) cells that have 70-75% reduction in sialic acid receptors (see abstract; Experimental Procedures; Results; and pages 16286 and 16287).

As set forth previously, the limitations 'wherein the mutant cell is selected for ..... molecules' in claim 1 represent process limitations. When claims are drawn to a product-by-process, claims are not limited to the manipulations of the recited step(s), but only the structure implied by the steps. MPEP § 2113 states:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)* (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicant has not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicant has not shown the underlying structure of the prior art mutant MDCK cell differs from that of the instantly claimed mutant cell.

That the prior art mutant cells contain reduced levels of terminal sialic acid, i.e., terminal N-acetylneuraminic acid, is inherent from the teachings of Martin *et al.* or Brandli *et al.* in light of what is well known in the art. For instance, it is well known in the art that the cell surface receptors that are recognized by influenza virus do contain terminal neuraminic (sialic) acids (see section 0054 of Doyle *et al.*). Martin specifically taught that the 70-75% reduced levels of cell surface sialic acid receptors present on the isolated mutant MDCK RCA^r (Madin-Darby canine kidney) cells are specific for influenza virus. It was also known in the art at the time of the invention that the neuraminic acid to which influenza virus preferentially binds is *N*-acetyl neuraminic acid linked to galactose by alpha(2-3) or alpha(2-6)Gal-*N*-acetylgalactosamine, the former specific to *Sambucus nigra* lectin and the latter specific to *Maackia amurensis* lectin. For example, see abstract and pages 3357 and 3358 of Ito *et al.* (*J. Virol.* 71: 3357-3362, 1997) which also taught that MDCK cells contain both the linkages (see abstract). Therefore, Martin's or Brandli's MDCK RCA^r cells are expected to bind to a lectin such as *Sambucus nigra* lectin and *Maackia amurensis* lectin.

As set forth previously, the disclosure of Martin *et al.* or Brandli *et al.* anticipates the instant invention. The reference of Doyle *et al.* or Ito *et al.* is **not** used as a secondary reference in combination with Martin *et al.* or Brandli *et al.*, but rather is used to show that every element of the claimed subject matter is disclosed by Martin *et al.* or Brandli *et al.*, because Doyle *et al.* or Ito *et al.* teach the recited inherent properties of the mutant cell. See *In re Samour* 197 USPQ 1 (CCPA 1978).

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

14) Claims 1, 3-6, 8-11 and 32-35 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claim 1 is confusing, internally inconsistent and/or fails to distinctly claim the subject matter. The following limitations are inconsistent in scope: 'cell comprising decreased levels of terminal sialic acid-containing host cell receptors for influenza virus relative to a corresponding wild-type cell' (see lines 1 and 2) and 'cell has decreased levels of *N*-acetylneuraminic acid and/or decreased levels of *N*-glycolylneuraminic acid relative to the corresponding wild-type cell' (lines 6-8). It is unclear whether the mutant cell has decreased levels of the broadly recited terminal sialic acid-containing host cell receptors, or decreased levels specifically of *N*-acetylneuraminic acid and/or *N*-glycolylneuraminic acid. Furthermore, the limitations 'sialic acid-containing host cell receptors' in lines 5 and 6 are inconsistent in scope with the limitation 'terminal sialic acid-containing host cell receptors' in line 2 of the claim.

(b) Claims 3-6, 8-11 and 32-35, which depend directly or indirectly from claim 1, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

15) Claims 1, 3, 9, 33 and 36 are rejected under 35 U.S.C. § 102(b) as being anticipated by Tazikawa *et al.* (JP 407203958A) as evidenced by Doyle *et al.* (US 20040132164, already of record).

Tazikawa *et al.* disclosed an isolated mutant CHO cell comprising reduced levels of N-glycolylneuraminic acid. The mutant strain is obtained by mutating a CHO cell and selecting a strain having reduced N-glycolylneuraminic acid compared to the parent CHO cell.
That the prior art mutant cell contains reduced levels of terminal sialic acid, i.e., terminal N-

acetylneuraminic acid, is inherent from the teachings of Tazikawa *et al.* in light of what is well known in the art. For instance, it is well known in the art that the cell surface receptors that are recognized by influenza virus do contain terminal neuraminic (sialic) acids (see section 0054 of Doyle *et al.*). The supporting of efficient influenza virus replication by wild-type mammalian or avian cell is not a property of the claimed mutant cell, but of the wild-type cell, which property is inherent to the wild-type cell. The property of resistance to growth inhibition by *Maakia amurensis* lectin or *Sambucus nigra* lectin, or supporting of the efficient replication by influenza virus with reduced sialidase activity, are considered as inherent properties inseparable from the prior art mutant cell. The prior art isolated mutant CHO cell comprising reduced levels of N-glycolylneuraminic acid is expected to have these functional properties.

Claims 1, 3, 9, 33 and 36 are anticipated by Tazikawa *et al.*

Objection(s)

16) For clarity, in line 5 of claim 1, it is suggested that Applicant replace the recitation 'sialic acid residues' with --sialic acid-containing residues--.

Remarks

17) Claims 1, 3-6, 8-11 and 32-36 stand rejected.

18) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300.

19) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

20) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may

be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

August, 2005

S. DEVI, PH.D.
PRIMARY EXAMINER